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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,727	08/30/2001	Kilian Dill	0405	1709
28869 7590 12/09/2008 COMBIMATRIX CORPORATION 6500 HARBOUR HEIGHTS PARKWAY MUKILTEO, WA 98275				
EXAMINER				
JUNG, UNSU				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/944,727

Applicant(s)

DILL, KILIAN

Examiner

UNSU JUNG

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2008.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10, 13 and 16-19 is/are pending in the application.
4a) Of the above claim(s) 19 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 10, 13 and 16-18 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 30 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/C)
Paper No(s)/Mail Date 4/29/02 & 5/30/06
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendments in the reply filed on September 29, 2008 is acknowledged and entered. The reply included amendments to the specification and claim 10.

Election/Restrictions

2. Applicant's election without traverse of species (d) (biotin/avidin, claims 10, 13, and 16-18) in the reply filed on September 29, 2008 is acknowledged.

Claims 10, 13, and 16-18 read on the elected species.

Status of Claims

3. Claims 10, 13, and 16-19 are pending, claim 19 has been withdrawn from consideration, and claims 10, 13, and 16-18 are currently under consideration for patentability under 37 CFR 1.104.

Priority

4. The instant application has a filing date of August 30, 2001 and does not claim for the benefit of a prior-filed application.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on April 29, 2002 and May 30, 2006 has been considered by the examiner. For the Wang et al. prior art reference in the IDS dated May 30, 2006, the volume number "127" has been included.

Oath/Declaration

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
The signature of the inventor, Kilian Dill is missing.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 10, 13, 17, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sosnowski et al. (U.S. Patent No. 6,051,380, Apr. 18, 2000) (hereinafter "Sosnowski") in view of Hill et al. (U.S. Patent No. 4,840,893, June 20, 1989) (hereinafter "Hill").

Sosnowski teaches a microarray device having addressable electrodes for detecting binding of a target molecule to a capture molecule (see entire document, particularly Abstract). The microarray includes plurality of addressable electrodes covered by a porous reaction layer (permeation layer) attached to the addressable electrodes and a plurality of capture molecules attached to the porous reaction layer at sites over the electrodes (Fig. 19). The microarray further includes a plurality of target molecules bound to the capture molecules (Fig. 19) and the target molecules are labeled with labels such as enzymes (oxidation/reduction enzymatic moiety) and biotin/avidin complexes (column 35, lines 36-41).

Regarding the limitation of "wherein the capture molecules are formed by in situ synthesis using electrochemical techniques using electrochemical reagents generated by the addressable electrodes and which electrochemically remove protecting groups during synthesis to locate the capture molecules at selected electrodes of the microarray, wherein electrophoresis is not used to attach the plurality of capture molecules at the sites corresponding to the electrodes, wherein the porous reaction

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layer allows electrochemically-generated protons to contact the capture molecules," MPEP states that the lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

With respect to claim 17, Sosnowski teaches that the capture molecules are oligonucleotides (column 30, lines 15-19).

With respect to claim 18, Sosnowski teaches that the target molecules are single-stranded DNA (column 6, lines 24-32).

However, Sosnowski fails to teach a microarray device, wherein the oxidation/reduction enzymatic moiety is attached to the target molecules through a biotin/avidin binding combination. Sosnowski also fails to teach a microarray device, further comprising a substrate molecule proximate to the oxidation/reduction enzymatic moiety, wherein the substrate molecule creates a local voltage signal when catalyzed by the oxidation/reduction enzyme through local generation of electrochemical reagents

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and a voltage signal measuring device electrically connected to each electrode on the microarray, wherein the voltage signal measuring device detects an electrical signal at each of the sites having capture molecules and the detection of the target molecules to the capture molecules is measured by different electrical signals at the sites having the target molecules and the sites not having target molecules.

Hill teaches electrochemical detection method (see entire document). Hill teaches that biotin bound to sample DNA/probe complex can be detected by addition of avidin to which a label such as enzyme is attached (column 1, lines 30-48). The enzyme can be detected by an enzyme substrate, which indicates the presence of the target molecules (column 1, Line 66-column 2, line 8). Hill further teaches that a voltage measuring device can be electrically connected to an electrode to detect electrical signal (voltage, column 6, lines 15-26).

With respect to claim 13, Hill teaches that the oxidation/reduction enzyme is horseradish peroxidase (column 10, lines 25-29).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the electrochemical detection method of Hill, which includes avidin attached to an oxidation/reduction enzyme, an enzyme substrate, and a voltage signal measuring device, in the microarray device of Sosnowski in order to measure target molecules bound to the capture molecules immobilized on each of the electrode in the microarray device. Since Sosnowski teaches that a variety of different detection techniques can be employed for the detection of target molecules, one of ordinary skill in the art at the time of the invention would have been motivated to

employ the electrochemical detection method of Hill with a reasonable expectation of success since the electrochemical detection method of Hill is compatible with the electrode microarray device of Sosnowski.

10. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sosnowski et al. (U.S. Patent No. 6,051,380, Apr. 18, 2000) (hereinafter "Sosnowski") in view of Hill et al. (U.S. Patent No. 4,840,893, June 20, 1989) (hereinafter "Hill") as applied to claim 10 above, and further in view of Choong et al. (U.S. Patent No. 6,518,024 B2, filed Dec. 13, 1999) (hereinafter "Choong").

Sosnowski in view of Hill teaches a microarray device for detecting binding of a target molecule to a capture molecule as set forth above. Although Sosnowski further teaches that the porous reaction layer can comprise variety of polymeric materials (column 2, lines 18-21), Sosnowski fails to teach that the porous reaction layer is made from dextran.

Choong teaches that thin layer of porous material that can be placed on top of an electrode can comprise variety of materials include dextran (see entire document, particularly column 7, lines 14-28).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to select an appropriate material for the porous reaction layer, since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. *In re Leshin*, 227 F.2d 197, 125 USPQ 416 (CCPA 1960).

See MPEP § 2144.07. Because the claimed device is known in the prior art and the prior art discloses that a variety of different materials can be used for the porous reaction layer of the device in general, the selection of a specific type of material for the porous reaction layer in itself does not present a novel feature of the claimed invention. Since one of ordinary skill in the art at the time of the invention would recognize that the a variety of known materials for making the porous reaction layer in the device of Hsieh Sosnowski in view of Hill, it would have been obvious to employ dextran for the porous reaction layer as taught by Choong in the device of Sosnowski in view of Hill.

Conclusion

11. No claim is allowed.
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is (571)272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Unsu Jung/
Unsu Jung
Patent Examiner
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